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Synthesis of moxifloxacin–Au (III) and Ag (I) metal complexes and their biological activities

Kondaiah Seku[1*], Anil Kumar Yamala[2], Mahesh Kancherla[3], Kishore Kumar K[4] and Vijayakumar Badathala[3]

Abstract

Background: The drug-metal complexes are used to control the growth of pathogens and parasites which are harmful to humans. Moxifloxacin (MOX) is a new fourth generation 8- methoxy fluoroquinolone. Its chemical name is [1-cyclopropyl-7-(S,S)-2,8-diazabicyclo(4.3.0)- non-8-yl-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3-quinoline carboxylic acid hydrochloride]. Many researchers have reported Moxifloxacin-metal complexes with transition metals and studied their biological applications. We have synthesized novel moxifloxacin- Au(III) and Ag(I) metal complexes ([Au(MOX) 2 (Cl) 2].2H 2 O and [Ag (MOX) 2].2H 2 O), characterized, and found their biological activities.

Methods: Moxifloxacin- Au(III) and Ag(I) metal complexes were prepared by adding corresponding aqueous solutions of Au(III) and Ag(I) metal salts to methanolic solution of Moxifloxacin. These metal complexes were characterized by physio-chemical techniques like UV-Vis, 1 H- NMR, FTIR, XRD, DSC, TGA, SEM and microanalytical data. The disc diffusion method was used to study the antibacterial activity of the Moxifloxacin-metal complexes.

Results: The structural assessment of these complexes has been carried out based on physio- chemical and spectroscopic methods. The powder X-ray diffraction data of the metal complexes revealed moderate crystallinity. SEM analysis confirms that [Ag(MOX) 2].2H 2 O complex has small rods like morphology whereas [Au(MOX) 2 (Cl) 2].2H 2 O has well crystalline rods like morphology. The results from DSC of moxifloxacin- Au(III) and Ag(I) metal complexes revealed the interaction between the drug and metals. Further, Au & Ag moxifloxacin metal complexes have shown significant antibacterial activity against gram-positive and gram-negative bacteria.

Conclusions: The spectral and analytical results clearly confirmed the coordination chemistry of Au (III) and Ag (I) Moxifloxacin metal complexes. The IR, electronic transition and elemental data led to the conclusion that the geometry of the complex of Au(III) is octahedral and that of Ag (I) complex is tetrahedral. The [Ag(MOX) 2].2H 2 O complex has showed good antibacterial activity compared to [Au (MOX) 2 (Cl) 2].2H 2 O metal complex. The antibacterial activity studies indicate the metal complexes have more biological activity than free ligand.

Keyword: Moxifloxacin-metal complexes, Gold, Silver, Structure, Biological activity

Background

Nowadays, most of the metal ions play an important role in many biological processes like biological function of proteins, and operating many regulation, stabilization, completion courses of cellular functions. The use of gold metal in complexation with drugs in modern, twentieth century medicine began with the discovery in 1890 by the German bacteriologist Robert Koch that gold cyanide K [Au (CN)$_4$] was bacteriostatic towards the *tubercle bacillus*. In 1920s, gold therapy was introduced for tuberculosis. Gold drugs have been used to treat a variety of diseases like psoriatic arthritis, a form of arthritis associated with psoriasis, juvenile arthritis, palindromic rheumatism, and discoid lupus erythematosus. Encouraging results have also been obtained with gold therapy as a treatment for various inflammatory skin disorders such as pemphigus, urticaria, and psoriasis (Thomas and Papandrea 1993).

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Table 1 UV-Vis spectra and magnetic moments of moxifloxacin–HCl and its complexes

Sample	Electronic bands, λ, nm				μeff	Geometry
	CT_{M-L}	$π–π^*$	$n–π^*$	$d–d$ transitions		
MOX.HCl	292	330	362	–	–	–
[Au(MOX)$_2$(Cl$_2$)].2H$_2$O	298	335	365	–	Paramagnetic	Octahedral
[Ag(MOX)$_2$]·2H$_2$O	295	339	369	600–750	Paramagnetic	Tetrahedral

*it idicates excitation

Silver compounds have been used in external preparations as an antiseptic, including both silver nitrate and silver proteinate, which can be used in dilute solution as eye drops to prevent conjunctivitis in newborn babies. Silver nitrate is also sometimes used in dermatology in solid stick form as a caustic ("lunar caustic") to treat certain skin conditions, such as corns and warts. Additionally, silver nitrate is used in certain laboratory settings to stain cells (Lansdown 2006; Kokura et al. 2010). Silver has also been used in cosmetics, intended to enhance antimicrobial effects and the preservation of ingredients.
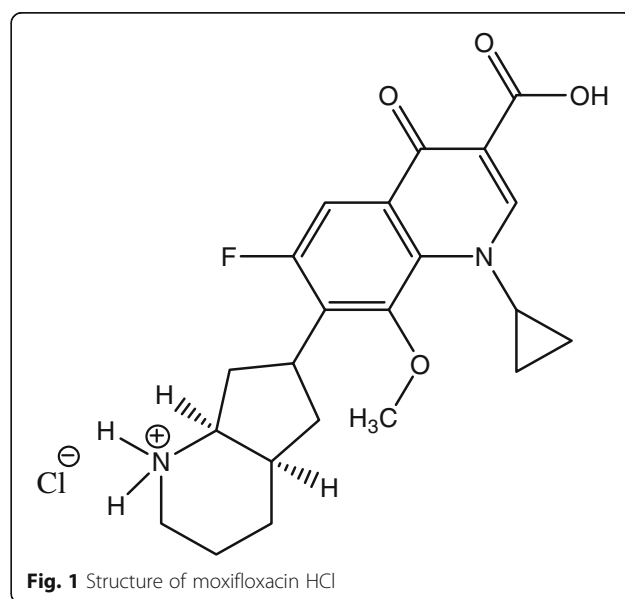
Researchers had a significant interest in the utilization of metal complexes as drugs to treat several human diseases. Metal and metal-drug complexes medicinal uses and their applications are increasing clinically for commercial importance. The preparation and characterization of the drug-metal complexes and evaluation (Sadeek et al. 2011; Power and Phillips 1993) of the biological activity have gained significance. According to chelation theory, chelation enhances the biological activity of metal complexes by increasing the complexity. Preparation of drug-metal complexes is of most significance in current days for curing of diseases by inhibition of growth of pathogens. It is clear from the recent literature that the trend towards the preparation of the drug-metal complexes has huge applications and will continue to occur in future medicinal applications (Ott 2009; Gasser et al. 2011; Maftei et al. 2015; Simon et al. 2005). However, the newly prepared drug-metal complexes have been more significant in present days, because they show good biological activity and these metal complexes find a role in detecting diseases (Neda et al. 2000; Filimon et al. 2010). The drug-metal complexes were also used to control the growth of pathogens and parasites which are harmful to humans.

Moxifloxacin (MOX) is a new fourth generation 8-methoxy fluoroquinolone (Fig. 1). Its chemical name is [1-cyclopropyl-7-(S,S)-2,8-diazabicyclo(4.3.0)-non-8-yl-6--fluoro-8-methoxy-1,4-dihydro-4-oxo-3-quinoline carboxylic acid hydrochloride]. The drug was developed mainly for the treatment of community-acquired pneumonia and upper respiratory tract infections. Moxifloxacin is also used for the treatment of hospital-acquired infections and has a very good safety and tolerability profile with trade names Avelox, Avalox, and Avelon. Moxifloxacin is to be considered a drug of the last remedy when all other drugs are failed. It inhibits DNA gyrase, a topoisomerase IV, and type II topoisomerase.

The investigators are well-known with the preparation of different metal complexes of moxifloxacin. W.F. El-Hawary et al. have reported spectrophotometric determination and biological activity of moxifloxacin.HCl. Sadeek et al. gave detailed study about the preparation and characterization of moxifloxacin metal complexes and their biological applications. Amina et al. have reported metal complexes of moxifloxacin–imidazole mixed ligands: characterization and biological studies. The majority of researchers reported about the preparation and characterization of the moxifloxacin-metal complexes with transition metals and studied their biological applications (Nakamoto et al. 1968; Soayed et al. 2013; Sultana et al. 2014).

However, reported literature has limited characteristics and investigations in the moxifloxacin-metal complexes. These metal complexes were shown moderate activity against gram-positive and negative bacteria. To our knowledge, no report is available in the literature about the synthesis and characterization of noble metal complexes of moxifloxacin. The development of
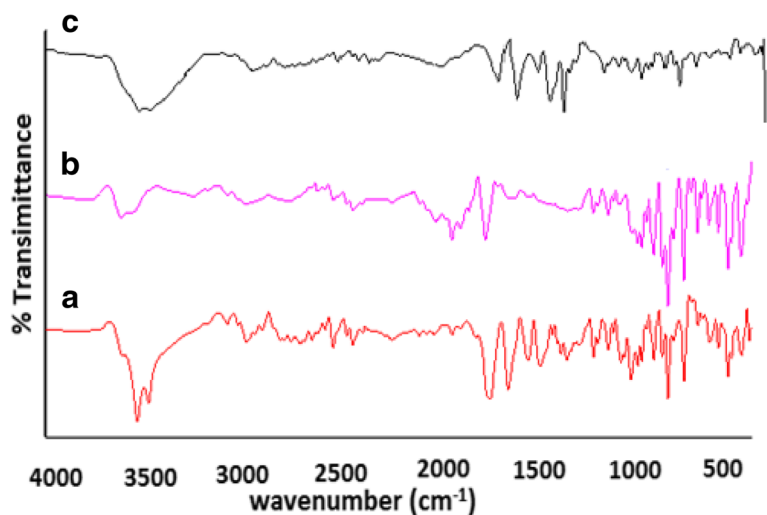

Fig. 1 Structure of moxifloxacin HCl

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Fig. 2 FTIR spectra of **a** moxifloxacin–HCl, **b** [Au(MOX)$_2$(Cl$_2$)].2H$_2$O, and **c** [Ag(MOX)$_2$]·2H$_2$O

noble metal-based drugs with promising pharmacological application may offer unique therapeutic opportunities (Rafique et al. 2010). The inorganic chemistry is provided with better opportunities to use the noble metal complexes (Mihorianu et al. 2016; Maftei et al. 2016a) as therapeutic agents on living organisms which is different from transition metals and non-metals. The noble metal-drug complexes have significant applications (Maftei et al. 2016b;

Neda et al. 1993a) in medicine and show a great diversity in action.

We report here synthesis and characterization of novel moxifloxacin–Ag(I) and Au(III) metal complexes, [Au(MOX)$_2$(Cl)$_2$].2H$_2$O and [Ag (MOX)$_2$].2H$_2$O. The synthesized moxifloxacin metal complexes were characterized by physio-chemical methods like UV-Vis, H^1-NMR, FTIR, XRD, DSC, TGA, and SEM. Antibacterial activity studies were carried out against
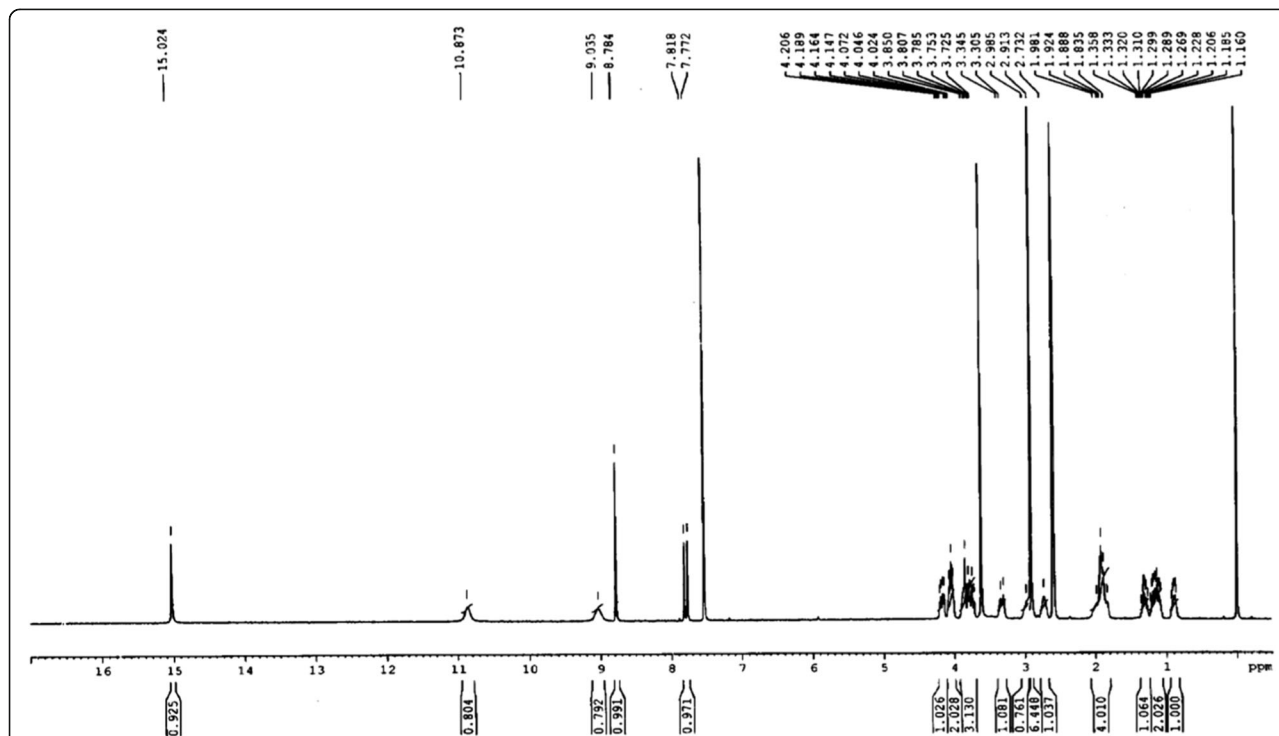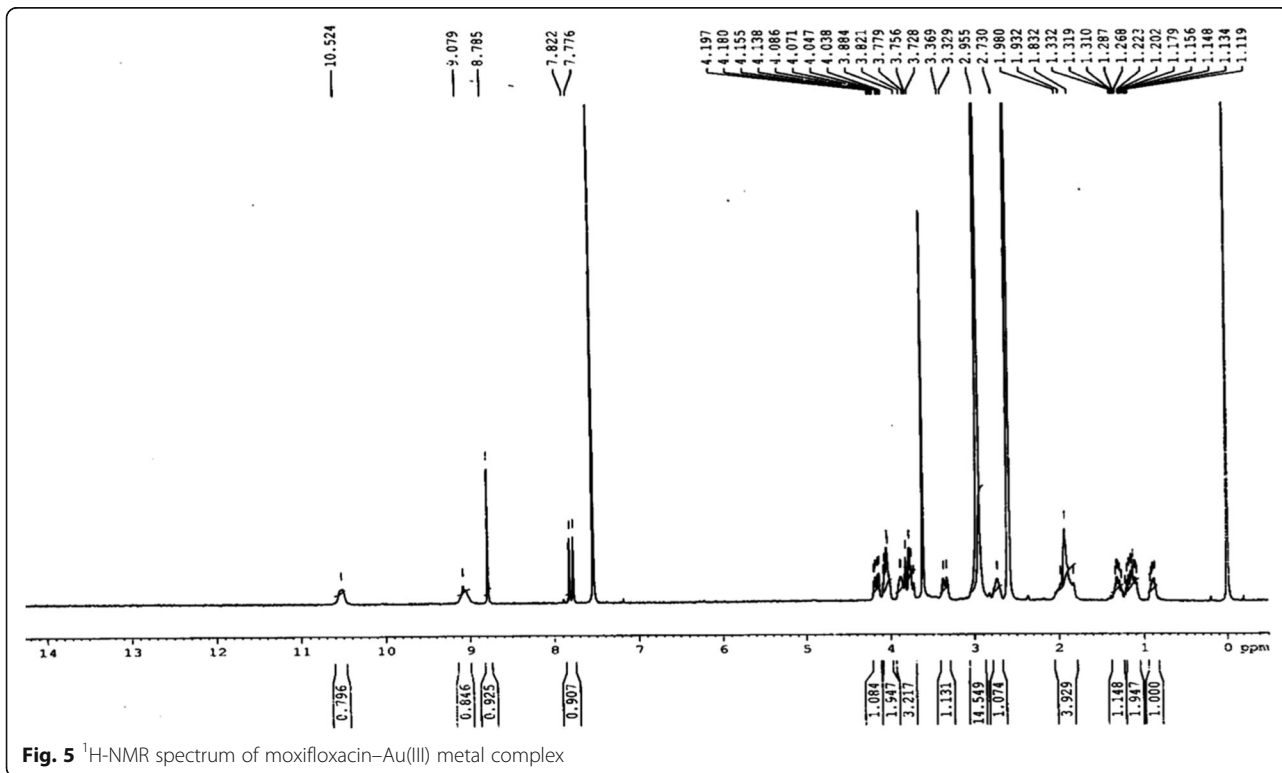

Fig. 3 ^{1}H-NMR spectrum of moxifloxacin–HCl
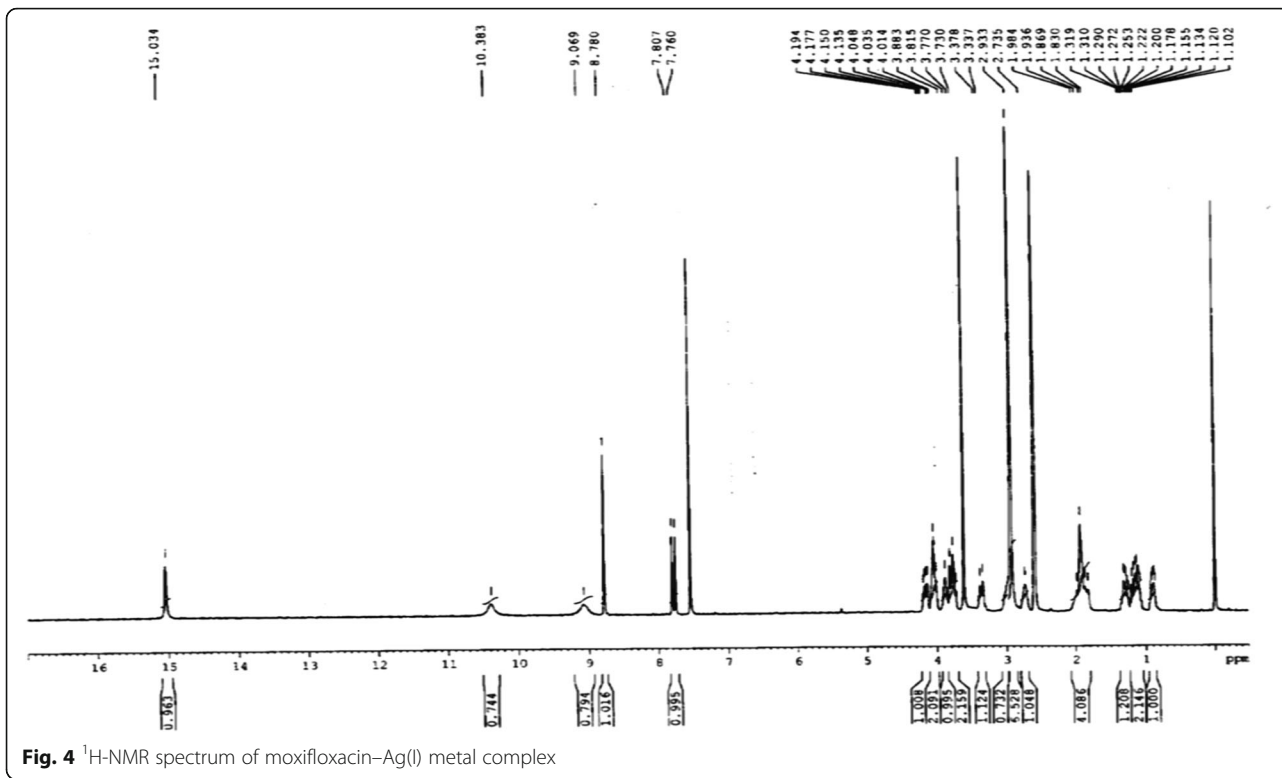
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Fig. 4 ^{1}H-NMR spectrum of moxifloxacin–Ag(I) metal complex

Fig. 5 ^{1}H-NMR spectrum of moxifloxacin–Au(III) metal complex

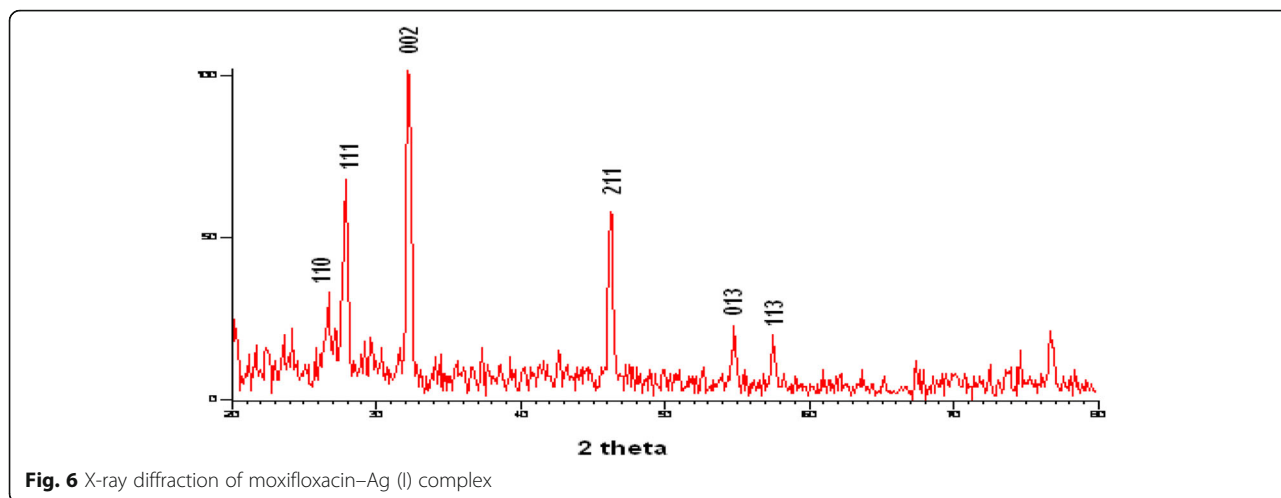Seku *et al. Journal of Analytical Science and Technology* (2018) 9:14

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Fig. 6 X-ray diffraction of moxifloxacin–Ag (I) complex

gram-positive and gram-negative bacteria for the prepared moxifloxacin metal complexes.

Methods

Materials

Moxifloxacin and gold(III) chloride were purchased from the Sigma-Aldrich Limited, India. Silver nitrate, methanol, and ether were purchased from MERK, India. All the chemicals and reagents are analytical reagent grade and were used without further purification. All glassware and magnetic stir bars were cleaned in an aquaregia solution ($3HCl$: HNO_3) and then cleaned with double distilled (DD) water.

Procedure for synthesis of Au (III) moxifloxacin metal complex

It was prepared by adding 1.6 g (0.01 M) amount of moxifloxacin ligand in 30 ml of methanol to the Au (III) ion (0.005 M) in distilled water and stirred about 12 h at 50 °C and cooled to room temperature. Yellow color precipitate of the metal complex was obtained with good yield. The precipitate was filtered and washed with hot water followed by cold methanol to free from unreacted metal salts and ligand. Finally, the residue was washed with ether and dried in a desiccator.

Moxifloxacin HCl

IR (KBr, cm^{-1}): 3530 (O–H stretching of HOH; COOH), 3156 (aromatic C–H stretching), 2978, 2800 (aliphatic C–H stretchings), 1709 (C=O stretching; COOH), 1620 (N–H bending), 1592, 1533 (aromatic C–C stretching), 1490 (C=C stretching), 1422, 1323 (aliphatic C–H bending), 1245 (C–F stretching), 1184 (C–O stretching), 1166 (C–N stretching), 1111 (C–C stretching), 1016, 991 (C–H bending; phenyl). ^{1}H NMR (DMSO) ppm: δ 10.87 (s,2H;NH_2^+), 9.03 (s,1H;COOH), 8.78 (s,1H;Ar–CH–), 7.81, 7.77 (s,1H, Ar–CH), 4.16, 4.14 (2H,H–2′,–CH_2), 4.07 (t,2H,H–4′,N–CH_2), δ3.85 (s,3H,–OCH_3), δ 3.72

(m,2H,H–3′,–CH_2), δ3.34 (t, 2H,H–1′,N–CH_2), δ 2.98 (s,1H, H–6′,N–CH–, diaserotopic), δ2.73(s,1H, H–7′,–CH–,diasteriotopic), 1.358 (t,1H,H–8′,–CH–), 1.088 (t,2H,H–9′,–CH_2), 0.934 (t,2H,H–10′–CH_2).

Moxifloxacin–Au(III) complex

Yield: 75%; IR (KBr, cm^{-1}): 3375 (O–H stretching), 3056 (aromatic C–H stretching), 2955, 2885 (aliphatic C–H stretchings), 1620 (N–H bending), 1525 (C=C stretching;phenyl), 1462 (aromatic C=C stretching), 1420, 1321 (aliphatic C–H bending), 1369 (N–H bending), 1325 (C–F stretching), 1189 (C–O stretching), 1080 (C–N stretching), 1049 (C–C stretching), 1031, 975 (C–H bending;phenyl).

^{1}H NMR (DMSO) δ ppm: 10.54 (s,2H;NH_2^+), 9.07 (s,1H;COOH), 8.78 (s,1H;Ar–CH–), 7.81, 7.77 (s,1H, Ar–CH), 4.16, 4.14 (2H,H–2′,–CH_2), 4.07 (t,2H,H–4′,N–CH_2), 3.85 (s,3H,–OCH_3), 3.72 (m,2H,H–3′,–CH_2), 3.34 (t, 2H,H–1′,N–CH_2), 2.98 (s,1H, H–6′,N–CH–,diasterotopic), 2.73 (s,1H,H–7′,–CH–,diasteriotopic), 1.35 (t,1H,H–8′,–CH–), 1.08 (t,2H,H–9′,–CH_2), 0.93 (t,2H,H–10′–CH_2).

Procedure for synthesis of Ag (I) moxifloxacin metal complex

It was prepared by adding required 1.6 g (0.01 M) amount of moxifloxacin ligand in 30 ml of methanol to

Table 2 X-ray diffraction data of moxifloxacin–Ag (I) complex

S. no.	*d* expt	*d* calc	2θ expt	2θ calc	h k l
1	3.476	3.467	26.701	25.869	110
2	2.924	2.833	27.91	30.574	111
3	2.704	2.452	32.34	33.619	002
4	2.036	2.002	46.24	45.257	211
5	1.692	1.733	54.83	53.754	013
6	1.605	1.634	57.53	56.428	113

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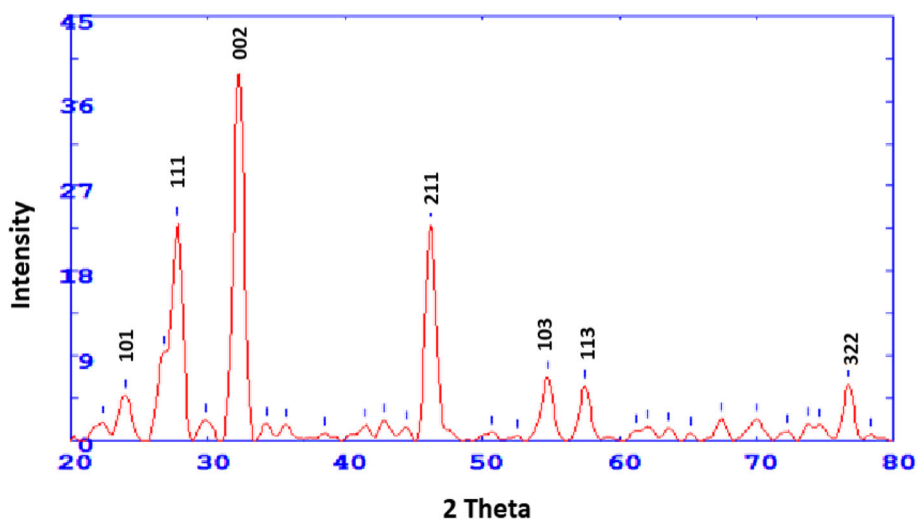
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Fig. 7 X-ray diffraction of moxifloxacin–Au(III) complex

the Ag (I) ion (0.005 M) in distilled water and stirred about 8 h. Light yellow color precipitate of the metal complex was obtained in good yield. The precipitate was filtered and washed with hot water followed by cold methanol to free from unreacted metal salts and ligand and finally with ether and dried in a desiccator.

Moxifloxacin–Ag(I) complex

Yield: 80%; IR (KBr, cm^{-1}): 3380 (O–H stretching), 3046 (aromatic C–H stretching), 2953, 2880 (aliphatic C–H stretchings), 1624 (N–H bending), 1516 (C=C stretching; phenyl), 1459 (aromatic C=C stretching), 1422, 1323 (aliphatic C–H bending), 1376 (N–H bending), 1320 (C–F stretching), 1185 (C–O stretching), 1084 (C–N stretching), 1051 (C–C stretching), 1030, 965, 877 (C–H bending;phenyl). ^{1}H NMR (DMSO) δ ppm: 10.38 (s,2H;NH$_2$$^+$), 9.06 (s,1H;COOH), 8.78 (s,1H;Ar–CH–), 7.80, 7.76 (s,1H, Ar–CH), 4.16, 4.14 (2H,H–2′,–CH$_2$), 4.07 (t,2H,H–4′,N–CH$_2$), 3.85 (s,3H,–OCH$_3$), 3.72 (m,2H,H–3′,–CH$_2$), 3.34 (t, 2H,H–1′,N–CH$_2$), 2.93 (s,1H, H–6′,N–CH–,diasterotopic), 2.73 (s,1H, H–7′,–CH–, diasteriotopic), 1.35 (t,1H,H–8′,–CH–), 1.08 (t,2H,H–9′,–CH$_2$), 0.93 (t,2H,H–10′–CH$_2$).

Characterization

The characterization of the synthesized moxifloxacin ligand and its metal complexes were recorded with UV-Vis-NIR spectrophotometer (UV-3600, Schimadzu) at 200–700 nm. FTIR analysis was carried out by KBr pellet method using JASCO FTIR 4600 in the scanning range of 450–4000 cm^{-1} used for recording spectrum. The powder XRD technique was used to study crystalline nature of the AuNPs by XRD (Rigaku, Miniflex) method with Cu kα (λ = 1.5418 Å) radiation. The morphology of the prepared moxifloxacin and its metal

complexes was examined by SEM. The ^{1}H NMR spectra of the ligand and its metal complexes were recorded on an AV-400 MHz NMR spectrometer in IICT, Hyderabad in DMSO-d$_6$ and CDCl$_3$ solvents at room temperature. Microanalysis data were obtained using a Carlo Erba EA1108 elemental analyzer. Thermograms were obtained using Perkin Elmer DSC 4000 differential scanning colorimeter at Vishnu Chemical, Hyderabad, India. Melting points were determined on the Kofler Hotstage microscope (Reichart Thermovar) and were uncorrected.

Biological activity studies

The disc diffusion method was used to study the antibacterial activity of moxifloxacin, and its gold(III) and silver(I) metal complexes. *B.Cereus*, *Pseudomonas Auruginosa*, *B. Subtilis*, and *E. coli* were used as model test strains. Prepared Luria-Bertani (LB) agar medium was transferred into sterilized Petri dishes and then solidified. Petri plates were spread with bacterial strains in a laminar airflow hood. Using micropipette, 10, 20, 30, and 40 μL of the AuNPs solution and 10 μL of streptomycin solutions were added to each well of all

Table 3 X-ray diffraction data of moxifloxacin–Au (III) complex

S. no.	*d* expt	*d* calc	2θ expt	2θ calc	h k l
1	3.638	3.567	24.44	24.25	101
2	2.924	2.853	28.60	29.21	111
3	2.704	2.652	32.52	31.88	002
4	2.036	2.012	46.43	45.65	211
5	1.692	1.683	54.13	53.75	103
6	1.600	1.585	57.53	56.95	113
7	1.217	1.213	78.48	78.23	322

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plates. They were dried in the laminar hood and incubated 24 h at 37 °C. All bacterial zones of inhibition were measured and assay was performed in triplicate.

Results and discussion

Electronic spectra and magnetic measurements

UV-Visible absorption spectral data of the moxifloxacin ligand and its moxifloxacin–Au(III) and moxifloxacin–Ag(I) metal complexes were shown in Table 1. The electronic transition of the ligand occurred at 292 nm (Table 3). But on complexation with the different metal ions like Au (III) and Ag (I), new bands appeared at 299 and 295 nm, respectively corresponding to the transitional charge transfer from the ligand to the different metal ions. Bands occurred in the region of 295 and 298 nm, respectively for $[Ag(MOX)_2]\cdot 2H_2O$ and $[Au(MOX)_2(Cl_2)]\cdot 2H_2O$ metal complexes (Sultana et al. 2014; Kondaiah et al. 2017) are assigned to charge transfer transition ($L \rightarrow M$). The magnetic moments of the present moxifloxacin of Au (III) and Ag (I) complexes are 1.80 and 1.75 BM, respectively. The magnetic moments of these ranges are suggested octahedral geometry for Au (III) and tetrahedral geometry for Ag

(I) complex (Kadyrov et al. 1996; Neda et al. 1996; Sonnenburg et al. 1994).

FTIR spectroscopic studies

The IR spectra of moxifloxacin ligand and its Au (III) and Ag(I) metal complexes were recorded by FTIR spectrophotometer (Kunze et al. 2002; Maftei et al. 2013; Neda et al. 1993b; Plinta et al. 1994). The FTIR spectra of the silver and gold complexes of moxifloxacin ligand exhibited major changes as compared to the free ligand. The strong bands at 1707 and 1624 cm^{-1} in the spectrum of moxifloxacin are assigned pyridone carbonyl and carboxyl stretches. In the FTIR spectra of Au (III) and Ag(I) complexes, the band at 1707 cm^{-1} was not recorded due to the formation of a bond between the metal ion and carboxylate oxygen (Fig. 2.) Two new bands are appeared for these complexes (Tulkens et al. 2012; Muhammad et al. 2007), at 1624 and 1335 cm^{-1}, 1620 and 1329 cm^{-1}, were assigned to asymmetric and symmetric $\upsilon(COO)$, respectively, for Ag (I) and Au (III)–moxifloxacin metal complexes. The difference values $[DV = \upsilon_{as}(COO) - \upsilon_s(COO)]$ of 289 and 290 for Au(III) and Ag (I) complexes respectively are used as an evidence for the bidentate chelation mode of the group. These results
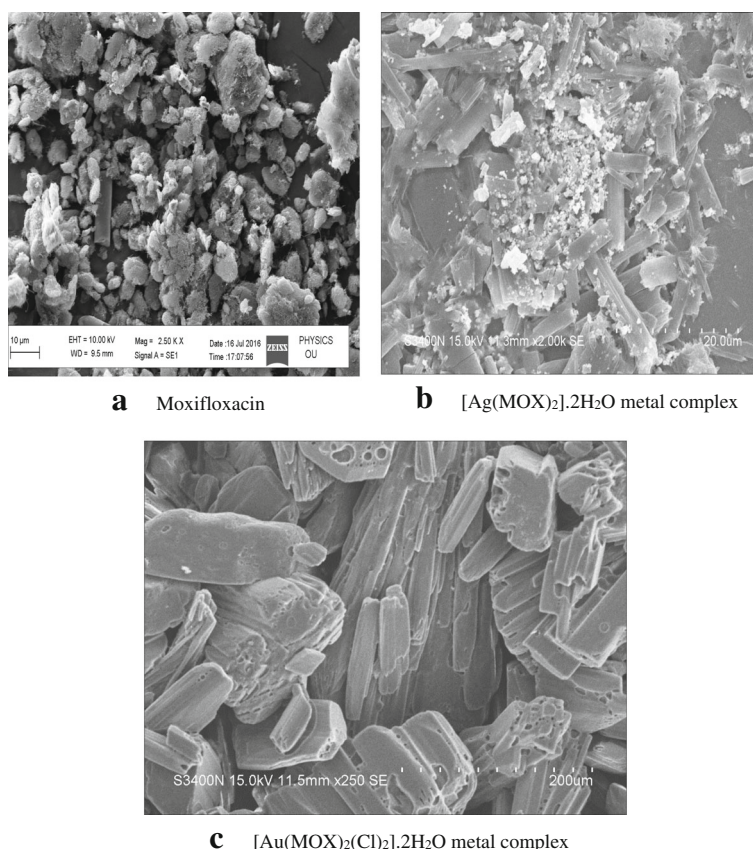

a Moxifloxacin

b $[Ag(MOX)_2]\cdot 2H_2O$ metal complex

c $[Au(MOX)_2(Cl)_2]\cdot 2H_2O$ metal complex

Fig. 8 SEM images of **a** moxifloxacin, **b** $[Ag(MOX)_2]\cdot 2H_2O$, and **c** $[Au(MOX)_2(Cl)_2]\cdot 2H_2O$ metal complexes

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revealed that the chelation of metals on moxifloxacin in this work.

¹H NMR spectroscopic studies

The proton NMR spectra of moxifloxacin Ag(I) and Au(III) metal complexes have been recorded in $CDCl_3$ and DMSO–d_6 and compared to the spectrum of moxifloxacin (Fig. 3). The moxifloxacin ligand ¹H NMR spectra, a broad singlet signal, were observed at δ 10.87 ppm corresponding to ($2H,NH_2^+$), and a strong singlet signal appeared at δ 9.03 ppm corresponding to –COOH. The aromatic protons that are H-2 and H-5 are very close to the coordination site of the moxifloxacin ligand. H-2 proton of moxifloxacin ligand appeared, strong singlet at δ 8.78 ppm and H-5 proton of moxifloxacin ligand noticed at (δ 7.81, 7.77 ppm) and appeared as a doublet. A triplet at (δ 4.18, 4.16, 4.14 ppm) due to [2H,N–4′–CH_2]. The H-1′and H-5′ protons were observed as doublet signal at (δ 4.07, 4.02 ppm), i.e., [4H,(2N–CH_2)], a singlet of 3H of OCH_3 group appeared at δ 3.85 ppm. The spectral band of [1H,8′–H] was shown at δ 3.30 ppm, a triplet at [4H (δ 2.98, 2.91, 2.73 ppm)] due to [4H (2H-2′, 2H-3′)] and (δ 1.28, 1.29, 1.35 and 0.93, 0.87 ppm)] due to [4H, (2H-9′, 2H-10′)]. Upon addition of a metal, these protons undergo the most significant changes. In the metal complexes, the H-2 proton gives a new signals at δ = 8.72 and 8.62 ppm while H-5 proton signals were appeared at δ 7.76 and 7.81 ppm, respectively, for Au (III) and Ag (II) moxifloxacin metal complexes (Figs. 4 and 5) (Chiririwa and Muzenda 2014; Ali et al. 2013; Efthimiadou et al. 2006). This shift is due to the complexation and difference in the configuration of complexes than ligand. In the ¹H NMR spectrum, a signal observed at δ 9.03 ppm due to carboxylic –OH proton in the ligand is shifted to δ 9.11 and 9.07 ppm respectively for Au (III) and Ag (II) moxifloxacin metal complexes.

Powder XRD studies of moxifloxacin metal complexes
Powder XRD studies of moxifloxacin–Ag (I) metal complex

The XRD patterns are used to explain qualitatively the degree of crystallinity. The diffractogram (6 diffractions) reflects between 20 and 80° (2θ) values (Fig. 6) for moxifloxacin–Ag (I) complex. All the peaks have been indexed 2θ values compared in the graph. On comparison, the values reveal that there is a good agreement (Arayne et al. 2005; Turel 2002) between values of 2θ and *d* values. The diffraction peaks observed at 2θ values 26.71, 27.91, 32.22, 46.25, 54.84, and 57.53° were indexed as (110), (110), (111), (002), (211), (013), and 113, respectively, as shown in Fig. 6. The maximum orientation observed at (002) at 2θ of 32.22 °. The formation of
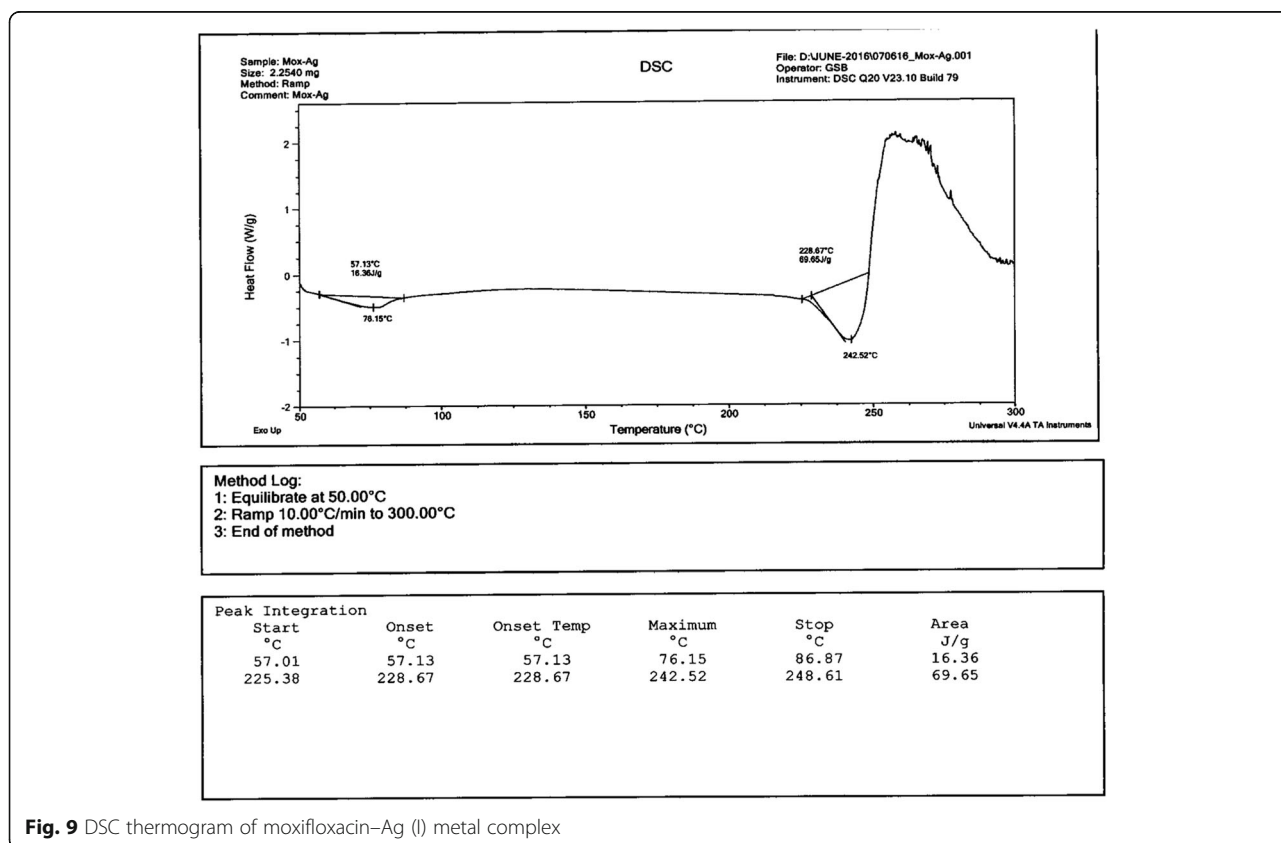

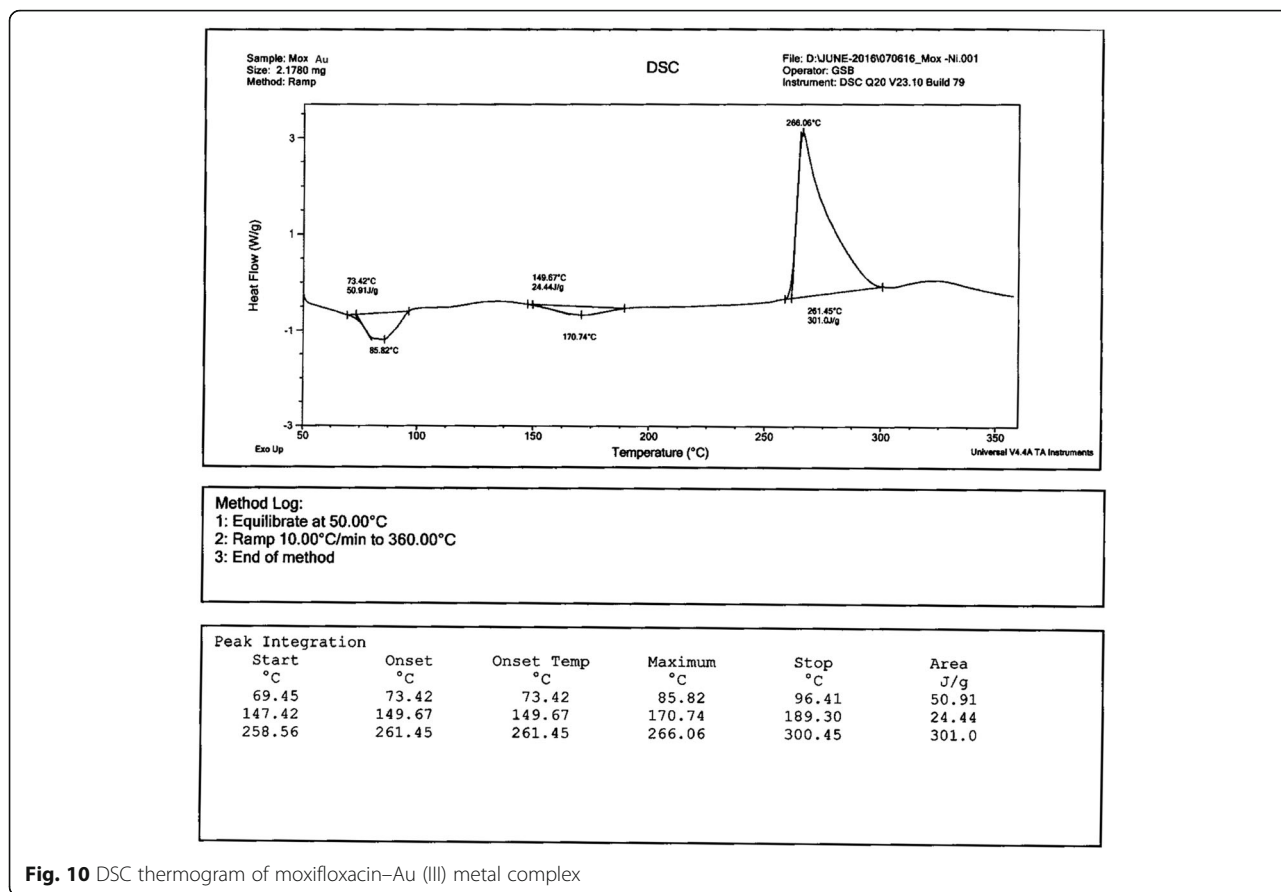**Fig. 9** DSC thermogram of moxifloxacin–Ag (I) metal complex

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Fig. 10 DSC thermogram of moxifloxacin–Au (III) metal complex

$[Ag(MOX)_2].2H_2O$ metal complex was confirmed by X-ray diffraction technique. These results agreed well with the standards of the Joint Committee on powder diffraction standards (JCPDS NO.01-072-0607). The X-ray diffraction data of MOX−Ag (I) complex are presented in Table 2. The powder X-ray diffraction data showed identical features with moderate crystallinity (Drevensˇek et al. 2006).

Powder XRD studies of moxifloxacin–Au (III) metal complex

The XRD patterns are used to explain qualitatively the degree of crystallinity. The diffractogram (6 diffractions) reflects between 20 and 80° (2θ) values (Fig. 7) for moxifloxacin–Au (III) complex. All the peaks have been indexed 2θ values compared in the graph. On comparison, the values reveal that there is good agreement between values of 2θ and d values. The diffraction peaks observed at 2θ values 24.44, 28.601, 32.52, 46.43,54.13, 57.53, and 78.48 ° were indexed as (101), (111), (002), (211), (103), (113), and (322), respectively, as shown in the Fig. 7. The formation of $[Au(MOX)_2(Cl_2)].2H_2O$ metal complex was confirmed by X-ray diffraction technique (De Almeida et al. 2007). These results are in good agreement with the standards of the Joint Committee on powder diffraction standards (JCPDS no. 04-0784). The X-ray diffraction data of MOX−Au(III) complex are presented in Table 3. The powder X-ray diffraction data showed moderate crystallinity.

Table 4 Thermal analytical data of the moxifloxacin metal complexes

Complex	Wt of the complex in mgs	Stage	Temp in range ^{0}C	Probable assignment	Mass loss (%)	Total loss (%)
$[Au(MOX)_2(Cl)].2H_2O$	4.147	1	145–320	Loss of $2H_2O$ and Cl_2molecule	5.44	87
		2	370	Loss of 2 L molecule	83.218	
		3	530	Corresponds to AuO	11.14	
$[Ag(MOX)_2].2H_2O$	4.245	1	140–325	Loss of $2H_2O$ and Cl_2 molecule	5.404	88
		2	490	Loss of 2 L molecule	78.816	
		3	500	Corresponds to AgO	15.64	

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Table 5 Analytical data of the moxifloxacin ligands and its metal complexes

Compound	Color	Yield in %	Melting point in ^{0}C	Elemental analysis							
				Carbon %		Hydrogen %		Nitrogen %		Metal %	
				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
MOX–HCl	Yellow	–	238–242	–	57.34	–	6.19	–	9.55	–	–
[Au (MOX)$_2$(Cl)$_2$].2H$_2$O	Yellow	75	255–266	49.25	49.12	5.40	5.15	8.85	8.78	6.12	6.05
[Ag (MOX)$_2$].2H$_2$O	Light yellow	80	242–250	46.39	46.10	5.44	5.20	10.21	10.05	15.05	14.95

SEM analysis

The SEM micrographs (morphology) of the moxifloxacin HCl have been taken in different magnification. The moxifloxacin HCl showed small needle-like morphology. [Ag(MOX)$_2$].2H$_2$O complex has shown small rods like structure whereas [Au(MOX)$_2$(Cl)$_2$].2H$_2$O showed well crystalline rod-like (Efthimiadou et al. 2008) structures (Fig. 8). The SEM micrographs of moxifloxacin metal complexes, [Au(MOX)$_2$(Cl)$_2$].2H$_2$O and [Ag(MOX)$_2$].2H$_2$O, reveal the structural modification, and it clearly indicates the formation of complexes.

Differential scanning colorimeter

DSC thermograms have shown an endothermic peak of moxifloxacin pure drug at 238.35 °C, which corresponded to its melting point. DSC thermograms (Figs. 9 and 10) of moxifloxacin–Au(III) and moxifloxacin–Ag(I) metal complex showed endothermic peaks at 261 and 228.67 °C, respectively (Khairnar and Singh 2016). The results of the thermograms obtained from DSC of moxifloxacin–Au(III) and Ag(I) metal complexes revealed the interaction between the drug and metals.

Thermal behavior of Au (III) and Ag (II) moxifloxacin metal complexes

The thermogravimetric studies of all the complexes were carried out in the air at a heating rate of 10 °C per minute. The thermoanalytical data are summarized in Table 4. The thermal decomposition of the complexes proceeds in three stages. Au (III) and Ag (I) complexes are thermally stable up to 132 and 138 °C, respectively. This table agreed with the elemental analysis of Table 5. The first stage of decomposition corresponds to endothermic dehydration of complexes by the loss of two

water molecules and chlorine occurs in the temperature range 145–320 and 140–325°C, respectively (Attimarad et al. 2012; Drevensˇek et al. 2006). The second decomposition with exothermic peak by the loss of ligand moiety occurs in the temperature at 490 and 492 °C, respectively. The solid residues above 530 and 500 °C were identified as Au and Ag metal oxides, respectively. In all the complexes, the final products are metal oxides (Chawla et al. 2012; Trindade et al. 2006).

The molar conductance of complexes in DMF ($\sim$ 10–3 M) was determined at 27 + 2 °C using systronic 303 reading conductivity bridge for Au(III) and Ag (I) complexes of moxifloxacin. These complexes are highly soluble in dimethylformamide (DMF). Therefore, these metal chelates are dissolved in DMF to perform conductivity measurements (El-Megharbel et al. 2015; Kljun et al. 2011; Khairnar and Singh 2016). A known amount of solid complex was transferred into 25 ml standard flask and dissolved in DMF. The contents were made up to the mark with DMF. The complex solution is transferred into a clean and dry 100 ml beaker. The molar conductance values of these metal complexes are measured and found to be 4.30 and 4.40 for Au (III) and Ag (II) complexes, respectively. These values suggest non-electrolytic nature (Gobec et al. 2014) of the present complexes.

The elemental analysis of moxifloxacin ligand and its metal complexes also performed; the compositions of the metal ligands with percentages calculated and found were tabulated in Table 5. The colored solid MOX–HCl complexes were stable in the air and insoluble in H$_2$O and most organic solvents except for DMSO and DMF upon gentle heating (Patel et al. 2011). The products were determined as non-electrolytes. The structures of MOX–HCl complexes were deduced as [Au(MOX)$_2$(Cl)$_2$].2H$_2$O and [Ag(MOX)$_2$].2H$_2$O.

Table 6 Antibacterial activities of moxifloxacin and its metal complexes

Complexes	Staphylococcus aureus	Bacillus subtillis	Streptococcus features	Pseudomonas aereuguinosa	Escherichia coli
MOX–HCl	8.40	27.50	25.61	8.40	18.31
[Au (MOX)$_2$(Cl)$_2$].2H$_2$O	14.30	12.11	10.15	13.50	15.45
[Ag (MOX)$_2$].2H$_2$O	15.24	17.16	15.20	15.20	25.65

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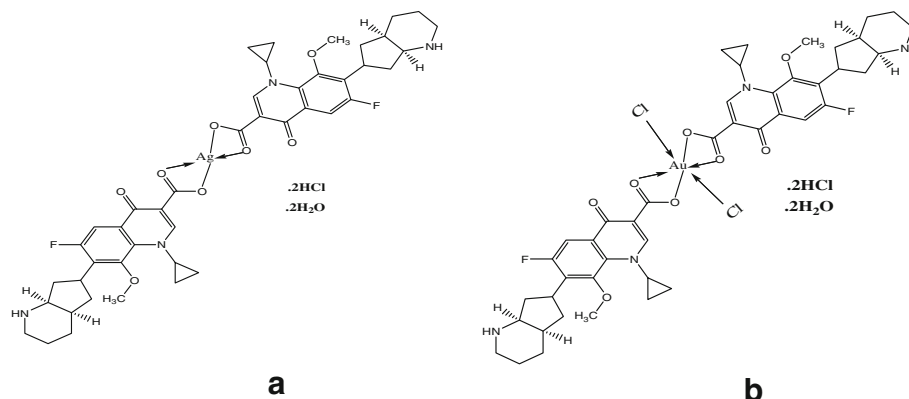
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Fig. 11 Proposed structures of moxifloxacin metal complexes. **a** Moxifloxacin–Ag(I) metal complex and **b** moxifloxacin–Au(III) metal complex

Antibacterial activity

The antibacterial activity of the moxifloxacin drug and its metal complexes (as a standard moxifloxacin) was tested against bacteria because bacteria can achieve resistance to antibiotics through biochemical and morphological modifications (Sultana et al. 2014; Mihorianu et al. 2016; Maftei et al. 2016a; Maftei et al. 2016b). The organisms used in the present investigations included *Staphylococcus aureus* (*S. aureus*), *Streptococcus features* (*S. features*) and *Bacillus subtillis* (*B. subtilis*) (as gram-positive bacteria) and *Proteus mirabilis* (*P. mirabilis*), *Pseudomonas aereuguinosa* (*P. aereuguinosa*), and *Escherichia coli* (*E. coli*) (as gram-negative bacteria). The zone of inhibition of moxifloxacin and its metal complexes against gram-negative and gram-positive bacteria were then evaluated by the well diffusion method (De Almeida et al. 2007; Efthimiadou et al. 2008; Patel et al. 2011; Singh et al. 2013; Tavares et al. 2004). The results of the bacterial screening of the synthesized compounds were recorded as shown in Table 6. The bacterial inhibition clear zones of both gram-positive and gram-negative bacteria can be observed around the well, while the zone of inhibition of moxifloxacin was moderate compared to all the metal complexes. Antibacterial activity of all the metal complexes significantly increased compared to the standard moxifloxacin. In these, moxifloxacin–Ag (I) metal complexes showed increased antibacterial activity compared to Au–moxifloxacin metal complexes (Nabd El-Wahed et al. 2009).

Conclusions

In this research work, novel Au(III) and Ag (I) moxifloxacin metal complexes were synthesized and characterized by magnetic susceptibility, elemental analysis, UV-Vis, FTIR, ^{1}H-NMR, TGA, DSC, and SEM. The spectral and analytical results clearly described the coordination chemistry of Au (III) and Ag (I) moxifloxacin metal complexes. The IR, electronic transition, and elemental data lead to the conclusion that the geometry of the complexes of Au(III) is octahedral and that of Ag (I) complex is tetrahedral structure. Hence, the structures of moxifloxacin metal complexes are given in Fig. 11. In all the complexes, the ligand acts as a bidentate. These metal complexes have shown significant antibacterial against the tested organisms. The [Ag (MOX)$_2$].2H$_2$O complex showed good antibacterial activity compared to [Au (MOX)$_2$(Cl)$_2$].2H$_2$O metal complex. The antibacterial activity indicates the metal complexes have more biological activity than free ligands. All the metal chelates are found to be non-electrolytes. These results will definitely encourage more research towards drug-metal complexes in medicine.

Authors' contributions

KS synthesized the moxifloxacin-silver and gold metal complexes. KS, MK, and VB characterized moxifloxacin and their metal complexes using FT-IR and H1NMR spectra. AY and KS characterized the moxifloxacin metal complexes using X-ray diffraction and SEM. SK and VB characterized the moxifloxacin metal complexes using electronic spectra, DSC, elemental analysis, and TGA. KKK conducted antibacterial studies on moxifloxacin and their metal complexes. All authors read and approved the final manuscript.

Ethics approval and consent to participate

NA

Consent for publication

NA

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Competing interests

The authors declare that they have no competing interests.

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